A cluster randomised trial of staff education, regular sedation-analgesia quality feedback, and a sedation monitoring technology for improving sedation-analgesia quality for critically ill mechanically ventilated patients.

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Word count (main text): 4380

ABSTRACT

Background

Optimum sedation of intensive care (ICU) patients requires the avoidance of pain, agitation, and unnecessary deep sedation, but achieving this is challenging. Excessive sedation can prolong ICU stay whereas light sedation may increase pain and frightening memories, which are commonly recalled by ICU survivors. We evaluated the effectiveness of three interventions that may improve sedation-analgesia quality: an online education programme; regular feedback of sedation-analgesia quality data; and use of a novel sedation-monitoring technology (Responsiveness Index, RI).

Methods

We did a cluster randomised trial in eight ICUs. These were randomly allocated to receive: education alone (two ICUs); education plus sedation-analgesia quality feedback (two ICUs); education plus RI monitoring technology (two ICUs); or all three interventions (two ICUs). A 45 week baseline period was followed by a 45 week intervention period, separated by an eight week implementation period in which the interventions were introduced. All mechanically ventilated patients were potentially eligible. We assessed patients' sedation-analgesia quality for each 12-hour nursing care period, and sedation-related adverse events (SRAEs) daily. Our primary outcome was the proportion of care periods with optimum sedation-analgesia, defined as free from excessive sedation, agitation, poor limb relaxation and poor ventilator synchronisation. Analysis used multilevel generalised linear mixed modelling to explore intervention effects in a single model taking clustering and patient level factors into account.

The trial is registered as Clinicaltrials.gov NCT01634451.

Findings

Between 1st June 2012 and 31st December 2014, we included 881 patients (9187 care periods) during the baseline period and 591 patients (6947 care periods) during the intervention period. During the baseline period optimum sedation-analgesia was present for 56·1% of care periods. We found a significant improvement in optimum sedation-analgesia with RI monitoring (OR 1·44 (95% CI: 1·07-1·95; p=0·017)) which was mainly due to increased periods free from excessive sedation (OR 1·59 (1·09-2·31)) and poor ventilator synchronisation (OR 1·55 (1·05-2·31)). However, more patients experienced SRAEs (RR 1·91 (1·02-3·58)). We found no improvement in overall optimum sedation-analgesia with education, but fewer patients experienced SRAEs (RR 0·56 (0·32-0·99)). The sedation-analgesia quality data feedback did not improve quality or safety. The statistical modelling predicted that for an average ICU patient a combination of responsiveness monitoring and online education increased the proportion of care periods with optimum sedation-analgesia by about 10% (from 61·6% to 72·3%) without increasing SRAEs.

Interpretation

Combining RI monitoring and online education has potential to improve sedation-analgesia quality and patient safety in mechanically ventilated ICU patients.

Funding

Chief Scientists Office, Scotland; GE Healthcare (Unrestricted funding).

INTRODUCTION

Deep sedation during mechanical ventilation in the intensive care unit (ICU) is associated with longer ICU stay, more infections, and higher mortality.[1] Strategies promoting lighter sedation can improve these outcomes but increase the risk of patient agitation and discomfort. Pain and frightening memories are widely reported by ICU survivors, and are associated with longer-term psychological problems, especially post-traumatic stress.[2-4] Guidelines recommend simultaneous avoidance of deep sedation, pain, and agitation, but changing staff behaviour to improve management is challenging.[3,5] Most previous trials have used protocols or daily sedation breaks, but the effectiveness of these interventions is uncertain and probably context specific.[6,7]

Sedation-analgesia management is a priority for improving ICU patient care.[8-10] Potential quality improvement strategies include staff education, regular feedback of sedation-analgesia quality data, and bedside sedation-monitoring technologies. Inadequate staff education is a known barrier to sedation-analgesia improvement,[11 12] and staff anxiety and increased workload from greater patient wakefulness may limit behaviour change.[5,13,14] Regular feedback of quality data has been successful in decreasing ICU-acquired infections, especially using process control methodology to track change over time.[15,16] However, the effectiveness of this approach has not been evaluated for improving sedation-analgesia quality. Although several bedside sedation-monitoring technologies exist, these have not previously been evaluated in large ICU effectiveness trials. Existing technologies were primarily developed to monitor depth of anaesthesia, their discriminant ability in the target sedation states during ICU care is limited, and they are only recommended in specific situations such as during neuromuscular paralysis. [3,17]

We developed three contrasting interventions that might improve sedation-analgesia quality in mechanically ventilated critically ill patients. First, an online evidence-based education resource; second, process feedback charts for tracking and regular feedback of sedation-analgesia quality; and third, a novel bedside technology designed to continuously monitor patients for possible deep sedation (Responsiveness Index (RI)).[18-22] We report a cluster randomised trial to evaluate the effectiveness of each of these interventions for improving sedation-analgesia quality in mechanically ventilated critically ill patients.

METHODS

The trial was part of a research programme funded by the Chief Scientist's Office Scotland (CZH/3/3) and with unrestricted support from GE Healthcare (Development and Evaluation of Strategies to Improve Sedation practice in inTensive care; DESIST, ClinicalTrials.gov NCT01634451)

Design

We did a cluster randomised trial in eight Scottish ICUs that admit mixed medical-surgical critically ill patients, excluding specialist cardiac, neurosurgical, or paediatric patients. We collected sedation-analgesia quality and other outcome data in all ICUs for 45 weeks (baseline period). We then randomly allocated ICUs to implement up to three interventions over an eight week period: online education ("education"); sedation-analgesia quality feedback ("process feedback"); and sedation monitoring technology ("responsiveness monitoring"). There were four pre-defined intervention combinations: education alone (two ICUs); education plus process feedback (two ICUs); education plus responsiveness monitoring (two ICUs); or all three interventions (two ICUs). Data were then collected for a further 45 weeks (intervention period). In a single analytic model we used a before-after approach (baseline versus intervention) to assess the effectiveness of education, and a parallel group factorial analysis to assess the effectiveness of process feedback and responsiveness monitoring, adjusting for potential confounders and outcomes observed in the baseline period. We evaluated effectiveness in clusters (ICUs) by analysing outcomes both at the care period level (12-hour nursing shift) and summarised at patient level. A process evaluation was included to further assess the impact of each intervention and to better understand the results. A detailed description of the study design, methodology, and analysis plan have been previously published.[23]

Setting and Participants

We selected ICUs in Scotland from teaching (N=4) and district general hospitals (N=4) that admitted between 202 and 798 mechanically ventilated patients annually (see http://www.sicsag.scot.nhs.uk). We selected ICUs to represent a typical UK case-mix. Nurse-patient ratio was 1:1 for mechanically ventilated patients consistent with UK national

guidance, and pre-trial approaches to sedation-analgesia management in each ICU are described in the supplement (table S1). We aimed to study patients requiring at least 24-48 hours of mechanical ventilation. Although interventions were at the ICU level the Adults with Incapacity (Scotland) Act 2000 required us to obtain consent from a relative/welfare guardian to collect data and include patients in the analysis. All mechanically ventilated, intubated patients were potentially eligible if consent was obtained within 48 hours of starting mechanical ventilation. Exclusion criteria were patients: no longer mechanically ventilated when screened or expected to be extubated within 4 hours; where active therapy was being withdrawn; and where the responsible clinician declined permission. Detailed screening logs captured enrolment rates and reasons for non-inclusion throughout the trial. The study was approved by the Scotland A Research Ethics committee (11/SS/0065).

Trial Interventions

Education: We delivered a nine module education package through the National Health Service provider of web-based educational materials (LearnPro NHS: http://www.learnpro.co.uk). Modules covered topics relating to sedation, analgesia, agitation, sleep, and delirium management in the ICU and included inbuilt assessments. Nurses completed training during the eight week implementation period, but the education package was available throughout the intervention period; it can be viewed at http://packagemanager.learnprouk.com (username “desisttest”; password “welcome”).

Process feedback: We developed statistical process control charts that described rates of overall optimum sedation, agitation, excessive sedation, poor relaxation, poor ventilator synchronisation, and patients experiencing sedation-related adverse events (SRAEs) at sequential two month intervals.[16,18] The methodology for this has been previously published.[18] We provided sedation-analgesia quality reports to ICUs randomised to this intervention during the eight week implementation period, and then updated reports every two months during the intervention period using ongoing trial data. ICUs were provided with strategies to share data from the reports (including posters and slide-sets) and encouraged to integrate these into quality improvement and other activities. An example of a report is included in supplementary material.

Responsiveness monitoring: We introduced a novel technology, Responsiveness Index (RI), into practice during the implementation period in the ICUs randomised to this intervention. RI is a continuous measure of patient arousal based on facial electromyography (fEMG) collected via frontal electrodes. The RI was colour-coded to indicate low arousal (red colour), intermediate arousal (amber colour), and higher arousal (green colour). The algorithm,[20] clinical validation studies,[21,22] and a proof of concept trial[19] have been published previously. Low arousal occurs during deep sedation, but also during natural sleep, low levels of clinical stimulation, and as a result of illness related coma. In the trial RI monitoring was intended to support bedside decision-making by clinical staff. Continuous RI monitoring was encouraged for all enrolled sedated patients. We asked nurses to use red RI values as a trigger to review sedation, reduce sedative doses, and transition patients into the amber/green RI range.

Outcomes

Our primary outcome was the proportion of care periods with optimum sedation-analgesia. We defined a care period as a 12 hours nursing shift and assessed sedation-analgesia with a quality assessment tool (SQAT) developed and validated prior to the trial.[18] The SQAT was implemented into routine daily practice in all ICUs prior to the baseline period and completed by staff at the end of each care period throughout the trial. We defined optimum sedation-analgesia as a care period free from excessive sedation, agitation, poor ventilator synchronisation, and poor relaxation. Care periods with each of the four quality components were reported as secondary outcomes.

Secondary patient level outcomes were the numbers of care periods *within each patient* with overall optimum sedation-analgesia and with each quality component.

Additional data were collected by research staff. Safety outcomes were the proportion of days during mechanical ventilation on which a SRAE occurred (defined as unplanned removal of nasogastric tube, central line, arterial line or drain; unplanned extubation; staff injury; or patient injury) and the proportion of patients who experienced SRAEs. Secondary outcomes were sedative and analgesic drug use (expressed as propofol and alfentanil equivalents), the proportion of days on which high dose (≥4000mg) propofol was administered (as a secondary safety outcome for risk of propofol-infusion syndrome), and

the proportion of patients receiving haloperidol (the first-line antipsychotic used for delirium management). Duration of mechanical ventilation, ICU and hospital stay, and ICU and hospital mortality were also recorded.

Sample Size

We did not know the rates of optimum sedation-analgesia and intraclass correlation coefficients (ICC) when designing the trial. We therefore modelled sample size to detect a 25% increase in the proportion of care periods with optimum sedation-analgesia with each trial intervention (power 80%; 2-sided significance level 5%) assuming a 70% optimum sedation-analgesia rate during baseline. We estimated sample size using a range of ICC (0.04 to 0.13) and patient numbers enrolled per ICU in each period (66 to 250). We re-checked power during the baseline period based on recruitment rates in participating ICUs. Our target sample size was 1600 patients (100 per ICU in both baseline and intervention periods). We estimated this would require 98 weeks per ICU (45 weeks baseline; 8 weeks implementation; 45 weeks intervention).

Randomisation and allocation concealment

ICUs started the study in a staggered manner to enable research team support during implementation. Randomised allocation was revealed to ICUs at the end of the baseline period to ensure allocation concealment. Randomisation used computer-generated random permuted blocks, stratified according to recruitment start date ("early": first four ICUs; "late": last four ICUs), to help balance numbers recruited across randomised groups.

Blinding

ICU and research staff were unaware of the intervention allocation during baseline data collection. As the trial aimed to modify behaviour we could not blind clinicians during the intervention phase. Clinical and research staff collected raw trial data every day as part of routine practice, but analysis to generate all trial outcome measures was done remotely by a statistician concealed from group allocation. Patients lacked mental capacity during the intervention and were unaware of ICU allocation.

Analysis

A detailed trial analysis plan was agreed prior to database lock.[23] We evaluated the effect of each intervention using multilevel generalised linear mixed models to account for the nested structure of the data, namely: care period (level one), within admission (level two), within ICU (level three). We planned to fit a three-level multilevel model, but if the nature of the data meant this was not feasible an alternative two-level multilevel model with care period (level one) and admission (level two) was pre-specified. We used Markov Chain Monte Carlo methods for parameter estimation and reported ICCs at admission and ICU levels.

We pre-defined a two-stage approach to analysis. First, an odds ratio (with 95% confidence interval (CI)) was calculated for the baseline to intervention change within *each* ICU, recognising that intervention uptake might vary between ICUs. At a pre-planned meeting, these data were reviewed by the independent data monitoring committee (IDMC) together with a report of qualitative process evaluation data that summarised uptake and engagement with interventions (prepared by a researcher (KK) blinded to quantitative data). The IDMC decided whether effects observed within individual ICUs supported proceeding to the pre-defined main analysis, which was a pooled analysis summarising overall intervention effects in the study.

Our primary analysis was a multilevel logistic regression. Fixed effect independent variables at the ICU level were: time period (baseline or intervention), interventions (process feedback and responsiveness monitoring), and intervention by time period interaction. Fixed effect independent variables at admission level were: age, sex, and APACHE II score (a measure of illness severity). We tested for an interaction between the process feedback and responsiveness monitoring interventions. Intervention effects were presented as odds ratios (95% CI). We did a pre-planned sensitivity analysis using intervention data recorded in the final 30 weeks of the study to check for sustained effects 4-5 months post-implementation. A detailed description of the analytic approach and the models used for the secondary outcomes have been published previously.[23]

Analyses used STATA (StataCorp; www.stata.com), MLwiN (University of Bristol; www.bristol.ac.uk/cmm/software/mlwin) and SAS (www.sas.com) statistical software.

In order to provide an illustration of the clinical impact of the interventions, we used mean age, sex and APACHE II score from the baseline period and the average treatment effects

from education, education plus process feedback, and education plus responsiveness monitoring observed in the trial to estimate the changes in sedation-analgesia quality and safety for an average ICU patient.

Process evaluation

For education we recorded the proportion of nursing staff completing online training in each ICU. To assess changes in knowledge, nurses answered ten core knowledge questions prior to starting education and repeated this at least five months after the implementation phase. Mean change in core knowledge test score was measured using analysis of covariance, adjusting for the pre-intervention score. For sedation-analgesia quality feedback we recorded the number of reports provided to ICUs during the intervention period. For responsiveness monitoring we recorded the number of patients monitored, duration of monitoring, and patterns of hourly RI data recorded by nursing staff.

An inductive thematic analysis of focus group data and field work undertaken in all ICUs throughout the study was undertaken by an ethnographic researcher (KK) and checked by an independent qualitative researcher (JH) according to a pre-specified plan. These data enabled detailed understanding of variation in the fidelity and reach of the intervention and staff perceptions across the ICUs. A description of the process evaluation design has been previously published and further details provided in supplementary material.[23]

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit.

RESULTS

Between 1st June 2012 and 31st December 2014, 881 patients were included during the baseline period and 591 patients during the intervention period. A summary of recruitment, patient demographics, and numbers of care periods with primary outcome data available for each ICU is shown in figure 1. Data describing admission diagnostic categories, and

additional detail concerning screening/enrolment are provided in supplementary material (table S2 and S3).

Our analysis of changes in sedation-analgesia quality in individual ICUs suggested variation in effects, with significant and potentially important changes between the baseline and intervention periods occurring in some ICUs. These are illustrated in supplementary material (figure S1). Our qualitative data suggested that this might be partly explained by differences in engagement with interventions between ICUs, including ICUs randomised to the same interventions. At the IDMC review members unanimously recommended undertaking the pooled main analysis to estimate overall effects from each intervention.

The baseline rates for overall optimum sedation-analgesia and for each of the sedation-analgesia quality components are shown in table 1. This showed that 56.1% of care periods had optimum sedation-analgesia prior to the interventions with relatively high rates of care periods free from unnecessary deep sedation (80·6%), agitation (90·1%), poor relaxation (82·7%), and poor ventilator synchronisation (89·2%).

Pooled raw data for the primary outcome prior to modelling indicating the number of patients and care periods available for analysis by phase and intervention are included in the supplementary material (table S4). These raw data suggested that there was no change (baseline to intervention) in rates of optimum sedation-analgesia associated with education or in the four ICUs that received process feedback, but an increase in optimum sedation-analgesia of 7·0% occurred in the ICUs randomised to responsiveness monitoring.

We found that ICU variance was small (ICC=0.003) suggesting a lack of clustering at ICU level, so we conducted multilevel modelling using a 2-level model. We also found no evidence for interaction between the process feedback and responsiveness monitoring interventions (p=0.08) so this interaction was excluded. The ICCs for all two-level analyses are shown in the supplementary material (table S5).

Results from modelling the effects of the interventions on the primary outcome and its components are summarised in figure 2. There was no statistically significant effect from education on overall optimum sedation-analgesia (OR 1.13 (95% CI: 0.86-1.48); p=0.392), but both days (RR 0.52 (0.30-0.92)) and patients (RR 0.56 (0.32-0.99)) with SRAEs decreased.

Responsiveness monitoring resulted in a significant improvement in optimum sedation-analgesia (OR 1.44 (1.07-1.95); p=0.017), which appeared to result from an increase in care periods free from excessive sedation (OR 1.59 (1.09-2.31)) and poor ventilator synchronisation (OR 1.55 (1.05-2.30)). Patient level analyses showed a similar pattern of findings (table 2A). In contrast, responsiveness monitoring appeared to increase patients experiencing SRAEs (RR 1.91 (1.02-3.58)). Process feedback demonstrated no beneficial effects on the optimum sedation-analgesia quality (OR 0.74 (0.54-1.00); p=0.052) or any secondary outcomes, and in the modelling there was a decrease in excessive sedation free care periods.

Other secondary outcomes are shown in tables 2B and 2C. We found no differences in average drug use per patient or length of mechanical ventilation, ICU or hospital stay, or mortality.

The effects we observed were similar in the sensitivity analysis restricted to data from the last 30 weeks of the intervention period (see table S6).

The predictions from modelling the effects of intervention combinations for an average ICU patient enrolled in the trial are shown in table 3. The modelling predicted that the combination of education and responsiveness monitoring resulted in a 10-11% improvement in the proportion of care periods with optimum sedation from 61.6% to 72.3%, mainly as a result of decreased deep sedation without an increase in SRAEs.

Process evaluation

Education: Most nurses completed the training during the implementation period (range 74% to 100% across the ICUs). Nursing knowledge increased from a mean pre-education score of 6.4 (SD 1.8) out of 10 by an average of 0.82 (95% CI: 0.65-0.98) adjusted for pre-education score (P<0.0001). The qualitative data suggested education was universally valued, considered comprehensive, and a useful resource especially for less experienced staff. Its impact appeared greatest on the awareness and management of agitation and delirium, and was perceived to increase nursing autonomy.

Process feedback: All four ICUs received the two-monthly sedation-analgesia quality reports as planned. However, qualitative data suggested process feedback was poorly understood and was sometimes disbelieved by staff especially when indicating poor sedation-analgesia quality. Process feedback had poor penetration within ICUs and was thought to lack relevance to daily bedside practice.

Responsiveness monitoring: Most enrolled patients were monitored (82% of enrolled patients; range 76% to 95% between the four ICUs). Monitoring initiation was delayed in many patients (median (1st, 3rd quartile) time between intubation and monitoring 21 hours (11, 34)), most likely while consent was obtained. The first RI value was red in most patients (59% overall; range 50-66% across ICUs) and remained red for a median 35% of monitored time (range 23 to 48% across ICUs). The median time to first achieving a green RI value was 9 hours (4, 23), suggesting nurses were not always acting on RI data or interventions to increase RI values were unsuccessful. The qualitative data suggested that many nurses found the technology a useful bedside prompt to review sedation management but views were mixed and some staff understood the monitor poorly, questioned its utility and validity, found its bedside presence intrusive, and did not alter their practice.

A more detailed summary of the process evaluation is presented in the supplement.

DISCUSSION

We found that optimum sedation-analgesia, meaning a patient was free from deep sedation, agitation, poor relaxation and poor ventilator synchronisation, was improved after implementing responsiveness monitoring technology. This intervention decreased the proportion of care periods with deep sedation and poor ventilator synchronisation, but increased SRAEs. A web-based education intervention did not affect overall optimum sedation-analgesia quality, but decreased SRAEs. The regular feedback of sedation-analgesia quality data did not improve outcomes or safety. Using statistical modelling, we estimated that the implementation of the education and responsiveness monitoring combination increased the absolute proportion of time with optimum sedation-analgesia by about ten percentage points for an average ICU patient without increasing SRAEs.

The most effective intervention, the responsiveness technology, was a continuous objective bedside alert to the possibility of deep sedation. Responsiveness Index is not linearly related to clinical sedation scores which was why we used it to assist decision-making rather than link values to strict protocols.[21] Sedation-analgesia quality improved mainly by decreasing deep sedation, consistent with the monitoring concept.[19-21] Our process evaluation found that monitoring was not started for >20 hours in more than half of patients and that red values occurred for prolonged periods despite guidance to review and decrease sedation. There was variable reach and penetration of the technology within ICUs consistent with delays in technology adoption. It is possible that greater improvements to sedation-analgesia quality with responsiveness monitoring might therefore be achieved with more education, experience and confidence in the technology and the use of decision-making protocols directly linked to RI data. The increase in SRAEs following introduction of responsiveness monitoring may have occurred because less time was spent with deep sedation. Concerns regarding agitation and adverse events are known to affect the willingness of nurses to decrease sedation.[13,14] Our data suggest responsiveness monitoring successfully changed the behaviour of bedside staff, although further work is required to maximise its uptake and clinical effectiveness.

The education intervention did not improve sedation-analgesia quality, but was associated with an almost 50% relative reduction in SRAE rates compared to baseline. This result was surprising, but is clinically important because adverse events may directly contribute to patient complications. Inadequate education and training are known barriers to sedation-analgesia improvement, and are difficult to overcome given the high staff numbers and turnover in many ICUs.[11,12] Specifically, increasing wakefulness through strategies such as daily sedation breaks is perceived to increase patient agitation, workload and nurse anxiety.[5,13,14] The management of pain, agitation and delirium was a strong focus of the education intervention and the process evaluation indicated that these elements were most positively perceived by staff, resulting in improved knowledge which was retained over time. Although this part of the analysis used a before-after approach, and it is possible that temporal trends contributed to the findings, the demonstration of improved knowledge, reduced SRAEs and the low cost of this intervention support its widespread implementation.

Process feedback did not improve any of the study outcomes and deep sedation appeared to increase over time. The modelling highlighted that the greatest improvements occurred in those ICUs not randomised to receive process feedback, especially those in which responsiveness monitoring was implemented. There did not appear to be any interaction between process feedback and responsiveness monitoring either statistically or in qualitative data from the process evaluation. The reach and fidelity of process feedback among staff was limited and it did not seem to impact bedside practice. We did not pre-define how the data should be used by ICUs and despite local meetings and champions it was poorly understood and lacked credibility with staff. Process control charts may be useful for tracking sedation-analgesia quality over time in response to sequential quality improvement initiatives, but our data suggest they are not effective in isolation.

The reasons that education and process feedback had no effect on the sedation-analgesia quality outcome were informed by our mixed-methods process evaluation. Quality improvement theory emphasises the need for interventions that engage staff in change especially in complex healthcare environments such as ICUs.[15] Although we included strategies to support implementation, staff perceived process feedback as too remote from the bedside and lacked relevance to individual patient management. In most ICUs staff did not appear to feel ownership of data, and often disbelieved "negative" findings. Education was positively perceived and improved knowledge, but it is possible that this was insufficient to change behaviours consistently and could have been limited by factors such as support from senior clinicians or perceived effect on workload. Although ICU-level effects on the sedation-analgesia quality outcome did not occur, the reduction in SRAEs suggested some behaviour change did occur. Responsiveness may have been more effective because it was present at the bedside and provided objective evidence to support clinical decision-making, thereby alleviating individual responsibility. Alternatively, the data may also have challenged clinicians resistant to change because the data were visible to colleagues. These mechanisms were supported by the process evaluation, which also suggested greater benefit might be possible with greater engagement with the technology.

Our primary outcome was the first integrated sedation-analgesia quality measure to include freedom from deep sedation, agitation, pain/discomfort, and poor ventilator synchronisation. Previous trials have used length of stay outcomes rather than patient

comfort.[6,7,24-26] In some of these trials the control groups were more deeply sedated than is current practice which may have inflated treatment effects, emphasising the importance of context and concurrent process evaluation in trials of complex healthcare interventions.[27] We chose sedation-analgesia quality as our primary outcome because this is important to patients, as highlighted in a recent UK public/professional priority setting partnership.[8] Baseline period data in our trial showed that freedom from excessive sedation was already present for 81% of care periods, suggesting the ICUs were already using a practice more consistent with evidence-based guidelines.[3] This is another possible explanation for the relatively small absolute treatment effects we observed. We found no differences in length of ventilation or ICU stay, but our trial was not powered for these outcomes and the baseline practice decreased the plausibility of a large effect on these outcomes. The improvements in sedation-analgesia and patient safety associated with education and responsiveness monitoring are potentially clinically relevant, especially if greater uptake than achieved in the trial were achieved through improved implementation strategies.

We used a cluster randomised design to compare the three interventions. This was efficient, enabled incorporation of baseline and intervention data from each ICU and a concurrent comparison of the effectiveness of the interventions. However, our trial has limitations. We could not blind clinical staff, which increased the risk of performance bias. We tried to minimise this by making relevant data recording part of routine care, analysing it remotely, concealing outcomes from staff (except when communicated as part of the process feedback intervention), and collecting a large volume of outcome data over a prolonged period. A sensitivity analysis undertaken using data collected >15 weeks after implementing interventions showed similar results suggesting sustained effects. The requirement for consent from a surrogate decision-maker was unavoidable within the Scottish legal/ethical system but increased the possibility of enrolment bias. We minimised this by randomising entire clusters and using the same consent process throughout the trial. This enriched the study population with patients requiring longer term ventilation, in whom the plausibility for effectiveness was highest. For example, the median duration of mechanical ventilation in the study population was 4 days compared to 2 days for all mechanically ventilated patients in participating ICUs (based on ICU audit data; see http://www.sicsag.scot.nhs.uk). Although we adjusted for relevant patient-level factors we cannot exclude the possibility of

unmeasured confounding variables. We also included a relatively small number of ICUs, especially for exploring several interventions, and it is impossible to exclude some temporal effect on the evaluation of online education with the design used. Variation between ICUs at baseline and differences in uptake and implementation of the interventions, which was suggested by the qualitative process evaluation, could also have been important. These issues are difficult to avoid in pragmatic cluster trials, but modelling enabled an estimation of overall effects. Our study illustrates the importance of a process evaluation in trials of complex healthcare interventions, to provide explanatory data to understand the effects observed.[27]

In conclusion, we have shown that continuous responsiveness monitoring can improve overall optimum sedation-analgesia quality in mechanically ventilated critically ill patients and that online staff education can decrease SRAEs. These interventions appear to have beneficial effects on staff behaviours in relation to sedation-analgesia and combining them may improve sedation-analgesia quality and patient safety in ICUs.

Contributors

TSW: Secured funding; literature search; protocol design; study management; data collection; data analysis; data interpretation; writing manuscript; approved final manuscript
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PP: Secured funding; study management; approved final manuscript

SC: protocol design; study management; data collection; approved final manuscript

TQ: protocol design; study management; data collection; approved final manuscript

JR: protocol design; study management; data collection; approved final manuscript

MMcD: protocol design; study management; data collection; approved final manuscript

AD: protocol design; study management; data collection; approved final manuscript

JR: protocol design; study management; data collection; approved final manuscript

JR: protocol design; study management; data collection; approved final manuscript

CJW: Secured funding; protocol design; study management; data analysis; data interpretation; writing manuscript; approved final manuscript

Declaration of interests

TSW received funding from GE Healthcare, who developed Responsiveness Index monitoring in collaboration with Edinburgh University, through unrestricted grants to Edinburgh University to undertake this work and studies preceding the trial during development of Responsiveness Index monitoring.

KU and PP are employees of GE Healthcare, who developed the Responsiveness Index technology. GE Healthcare provided unrestricted grant funding for the project as co-funder with the Chief Scientists Office (Scotland) through a grant to Edinburgh University (who co-sponsored the trial with NHS Lothian). They had no role in data analysis, interpretation, or writing the manuscript.

CJW was supported in this work by NHS Research Scotland via the Edinburgh Health Services Research Unit.

No other authors declare relevant conflicts of interest

Acknowledgments

The trial was funded by a grant from the Chief Scientists Office, Scotland (CZH/3/3) and with an unrestricted grant from GE Healthcare. GE Healthcare provided all of the Responsiveness Index monitors and associated disposables used in the trial.

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560

561 **Research in context**

562 **Evidence before this study**

563 We searched Pubmed, Medline and the Cochrane Database of Systematic Reviews database
564 without language or date restrictions for published research that evaluated interventions to
565 improve sedation and analgesia quality for mechanically ventilated intensive care patients.
566 We also searched recently published guidelines relevant to sedation and analgesia
567 management. The most recent search was done on January 27th 2016. Published trials focus
568 on avoidance of deep sedation rather than integrated measures of sedation depth, pain,
569 and agitation. Recent research with patients suggests optimising overall comfort is
570 important, and observational research indicates pain and discomfort are prevalent. The
571 primary outcome for most randomised trials was length of mechanical ventilation or ICU
572 stay rather than patient-focussed outcomes. Two recent Cochrane reviews summarised
573 existing RCT evidence. Aitken found that evidence supporting protocol-driven sedation did
574 not support effectiveness for reducing duration of ventilation or ICU stay. Burry did not find
575 strong evidence to support daily sedation interruptions for reducing duration of ventilation
576 or ICU stay. Both studies highlighted the importance of the context and setting for
577 understanding the generalisability of trial results. Although some sedation-monitoring
578 technologies exist, they are largely designed for depth of anaesthesia monitoring and their
579 discriminant value is limited for ICU sedation. Existing technologies have not been tested in
580 large randomised trials.

Added value of this study

This cluster randomised trial evaluated the effects of three differing interventions that might improve sedation-analgesia quality in mechanically ventilated patients: an online educational programme for staff, the regular feedback of data about ongoing sedation-analgesia quality, and a novel sedation-monitoring technology (Responsiveness Index) developed as a continuous alert for possible deep sedation. The study used sedation-analgesia quality as the primary outcome, whose components were the absence of unnecessary deep sedation, agitation, and two discomfort behaviours (poor relaxation and poor synchronisation with the ventilator). An embedded process evaluation showed variation in the reach and uptake of the interventions between ICUs, despite clear implementation strategies. Despite this, we found that the Responsiveness Index monitoring was most effective at increasing rates of optimum sedation, mainly by decreasing deep sedation and poor ventilator synchronisation. We found that education did not change the primary outcome but improved patient safety by decreasing sedation-related adverse events. Regular feedback of sedation-analgesia quality data alone did not improve quality.

Implications of all the available evidence

Our findings suggest that using continuous Responsiveness Index monitoring can help decrease deep sedation and improve overall optimum sedation. Combining this with system level staff education may enable ICUs to decrease deep sedation while maintaining patient safety. This approach might overcome some of the barriers to changing sedation practice in ICUs. A trial designed to determine whether Responsiveness Index monitoring can improve outcomes such as length of stay and cost-effectiveness in addition to sedation-analgesia quality is justified

TABLES

Table 1: Total number of care periods with data available on each sedation-analgesia quality measure during baseline period for all eight participating ICUs, along with the number and percentage of care periods with optimum sedation-analgesia and each component of the primary outcome.

Sedation-Analgesia Quality Measure	Total number of evaluable care periods	Number of care periods with measure	% of care periods with measure
Primary Outcome			
Optimum Sedation	9187	5150	56·1
Components of Primary Outcome			
Free from Excessive Sedation	9319	7510	80·6
Free from Agitation	9274	8360	90·1
Free from Poor Relaxation	9362	7744	82·7
Free from Poor Synchronisation	9335	8331	89·2

Table 2A: Estimates of effects of each intervention on the sedation-analgesia quality measures at patient level. A rate ratio (RR) >1 indicates an increase in the outcome with the intervention (improvement).

		Education	Process Feedback	Responsiveness Monitoring
Sedation-Analgesia Quality Outcomes at Patient Level				
Optimum Sedation	RR (95% CI)	1·02 (0·92-1·13)	0·90 (0·80-1·01)	**1·17 (1·04-1·31)**
Free from Excessive Sedation	RR (95% CI)	1·02 (0·96-1·08)	**0·90 (0·84-0·97)**	**1·09 (1·01-1·17)**
Free from Agitation	RR (95% CI)	1·02 (0·96-1·08)	1·02 (0·95-1·09)	0·98 (0·91-1·05)
Free from Poor Relaxation	RR (95% CI)	0·98 (0·92-1·04)	0·98 (0·91-1·05)	1·05 (0·98-1·13)
Free from Poor Synchronisation	RR (95% CI)	1·00 (0·95-1·07)	0·99 (0·92-1·06)	1·04 (0·97-1·11)

Note: Outcomes with statistically significant intervention effects (95% confidence intervals (CIs) do not overlap 1) are highlighted in bold. Results are from generalised linear model with log link and negative binomial error distribution for number of DESIST care periods with an outcomes present for each patient, using the total number of DESIST care periods with valid data for that outcome for each patient as an offset. Adjusted for age, sex and APACHE II score.

Table 2B: Estimates of effects of each intervention on the sedative and analgesic drug use outcomes. A ratio of geometric means (RoGM) or odds ratio (OR) <1 indicates a decrease in the outcome with the intervention (improvement).

		Education	Process Feedback	Responsiveness Monitoring
Sedative and Analgesic Drug Use				
Propofol Equivalents Used (mg)	RoGM (95% CI)	1·09 (0·85-1·40)	1·01 (0·77-1·34)	1·01 (0·76-1·34)
Alfentanil Equivalents Used (mg)	RoGM (95% CI)	1·06 (0·83-1·35)	1·05 (0·80-1·38)	1·18 (0·90-1·55)
Day on which ≥4000mg Propofol (or equivalents) Administered	OR (95% CI)	**0·43 (0·22-0·86)**	**2·45 (1·11-5·42)**	1·11 (0·52-2·38)
Patient Received Haloperidol	OR (95% CI)	1·18 (0·74-1·89)	0·95 (0·56-1·63)	1·14 (0·68-1·91)

Note: Outcomes with statistically significant intervention effects (95% confidence intervals (CIs) do not overlap 1) are highlighted in bold. Results are from normal linear model for log-transformed propofol and alfentanil equivalents, mulitlevel generalised linear model with logit link for day on which ≥4000mg propofol (or equivalents) administered, and generalised linear model with logit link for patient received haloperidol. Adjusted for age, sex and APACHE II score.

Table 2C: Estimates of effects of each intervention on patient outcomes. For mortality outcomes an odds ratio (OR) <1 indicates a reduction in mortality with the intervention (improvement). For the time to event outcomes a hazard ratio (HR) >1 indicates an increased risk of the event with the intervention (improvement), which corresponds to a shorter duration of mechanical ventilation, ICU stay, or hospital stay.

		Education	**Process Feedback**	**Responsiveness Monitoring**
Mortality				
ICU	OR (95% CI)	1·19 (0·73-1·93)	1·33 (0·77-2·29)	0·78 (0·46-1·35)
Hospital	OR (95% CI)	1·08 (0·68-1·72)	1·08 (0·65-1·81)	0·82 (0·50-1·37)
Time-To-Event Outcomes				
Cessation of Mechanical Ventilation	HR (95% CI)	0·92 (0·76-1·12)	1·00 (0·80-1·24)	0·87 (0·70-1·08)
Discharge from ICU	HR (95% CI)	0·89 (0·71-1·11)	0·98 (0·77-1·26)	0·92 (0·71-1·17)
Discharge from Hospital	HR (95% CI)	0·88 (0·70-1·11)	1·15 (0·89-1·48)	1·03 (0·79-1·33)

Note: Outcomes with statistically significant intervention effects (95% confidence intervals (CIs) do not overlap 1) are highlighted in bold. Results are from generalised linear model with logit link for ICU and hospital mortality and a Cox proportional hazards model for time to event outcomes (durations of mechanical ventilation, ICU and hospital stay). Adjusted for age, sex and APACHE II score. The proportional hazards assumption was assessed by testing for a non-zero slope over time on the basis of Schoenfeld residuals.

Table 3: Predicted percentages from modelling effects of intervention(s) on sedation-analgesia quality measures at care period level and sedation-related adverse event (SRAE) outcomes.

	Baseline	Education	Education + Process Feedback	Education + Responsiveness Monitoring
Sedation-Analgesia Quality Measure at Care Period Level				
Primary Outcome				
Optimum Sedation	61·6%	64·4%	57·1%	72·3%
Components of Primary Outcome				
Free from Excessive Sedation	85·5%	86·5%	80·6%	91·0%
Free from Agitation	97·3%	97·6%	98·1%	97·2%
Free from Poor Relaxation	90·3%	88·6%	88·4%	90·7%
Free from Poor Synchronisation	94·5%	94·8%	94·3%	96·6%
Sedation-Related Adverse Events				
Day on which a SRAE Occurred	2·0%	1·1%	1·1%	1·9%
Patient Experienced a SRAE	17·6%	10·7%	12·1%	18·6%

Note: Predictions are for the average ICU patient enrolled in the study (age 60 years, 60% male, APACHE II score 22).

Figure 1: Modified CONSORT diagram to show the flow of patients included in each ICU during the baseline and intervention periods of the study, together with characteristics of the patients. Further detailed screening data are included in the supplementary material (Table S3).

Figure 2: Estimates of effects of each intervention, odds ratios (OR) and 95% confidence intervals, on sedation-analgesia quality measures at care period level and sedation-related adverse event (SRAE) outcomes. For the sedation-analgesia quality measures an OR >1 indicates an increase in the outcome with the intervention (improvement); for the SRAE outcomes an OR <1 indicates a decrease in the outcome with the intervention (improvement).

Note: Results are from multilevel generalised linear model with logit link for sedation-analgesia quality measures and SRAE at day level, and generalised linear model with logit link for SRAE at patient level. Adjusted for age, sex, and APACHE II score.

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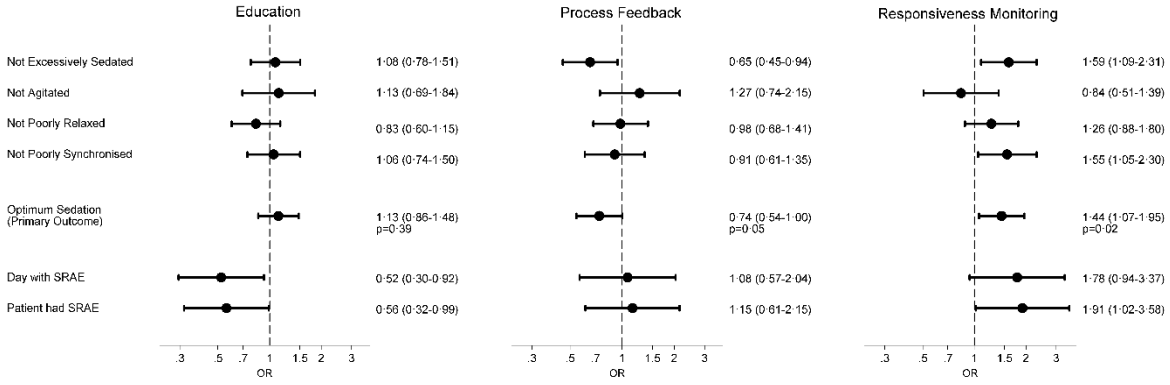
Figure 1

			ICU 1	ICU2	ICU 3	ICU 4	ICU 5	ICU 6	ICU 7	ICU 8
45 WEEKS	**BASELINE PERIOD**									
	Screened	(N)	1225	483	1015	408	374	282	722	315
	Eligible	(N)	206	190	453	274	135	141	223	106
	Consented	(N (%))	120 (58)	98 (52)	236 (52)	103 (38)	108 (80)	61 (43)	92 (41)	74 (70)
	Excluded	(N)	2	0	0	1	1	0	5	2
	Primary outcome data available	(N (%))	113 (96)	91 (93)	232 (98)	101 (99)	104 (97)	61 (100)	78 (90)	67 (93)
	Age	(mean (SD))	59 (16)	61 (16)	59 (16)	58 (17)	64 (17)	58 (14)	60 (14)	59 (15)
	Male	(%)	67	52	61	67	54	57	66	61
	APACHE II score	(mean (SD))	22 (8)	21 (8)	23 (7)	24 (7)	20 (7)	24 (8)	24 (8)	23 (8)
	Care periods with primary outcome data	(N)	1401	1127	2350	1407	717	559	923	703
8 WEEKS	**IMPLEMENTATION PERIOD**		**Education**		**Education + Process Feedback**		**Education + Responsiveness Monitoring**		**Education + Process Feedback + Responsiveness Monitoring**	
45 WEEKS	**INTERVENTION PERIOD**		**ICU 1**	**ICU2**	**ICU 3**	**ICU 4**	**ICU 5**	**ICU 6**	**ICU 7**	**ICU 8**
	Screened	(N)	1105	369	944	345	244	191	394	209
	Eligible	(N)	118	120	306	163	90	81	201	63
	Consented	(N (%))	65 (55)	58 (48)	170 (56)	55 (34)	62 (69)	28 (35)	116 (58)	44 (70)
	Excluded	(N)	0	0	2	1	0	0	4	0
	Primary outcome data available	(N (%))	64 (99)	56 (97)	167 (99)	52 (97)	61 (98)	28 (100)	107 (96)	42 (96)
	Age	(mean (SD))	60 (17)	60 (15)	59 (15)	59 (18)	67 (14)	65 (12)	58 (14)	56 (18)
	Male	(%)	54	53	67	52	60	46	56	73
	APACHE II score	(mean (SD))	20 (7)	21 (7)	22 (8)	24 (7)	20 (7)	26 (6)	23 (8)	24 (8)
	Care periods with primary outcome data	(N)	841	589	2149	510	511	281	1383	683

Figure 2



A cluster randomised trial of staff education, regular sedation-analgesia quality feedback, and a sedation monitoring technology for improving sedation-analgesia quality for critically ill mechanically ventilated patients (DESIST trial).

SUPPLEMENTARY MATERIAL

Table S1: Summary of the sedation and pain assessment tools used by each of the ICUs, and their approach to using sedation holds and/or reducing sedation prior to starting the trial.

	Education		**Education + Process Feedback**		**Education + Responsiveness Monitoring**		**Education + Process Feedback + Responsiveness Monitoring**	
	ICU1	**ICU2**	**ICU3**	**ICU4**	**ICU5**	**ICU6**	**ICU7**	**ICU8**
Sedation assessment tool	RASS	RAMSAY	RASS	RASS	RASS	SAS	RASS	RASS
Delirium monitoring	CAM-ICU twice daily	NO	CAM-ICU twice daily	CAM-ICU twice daily	NO	No consistency	CAM-ICU	CAM-ICU
Pain assessment tool for mechanically ventilated patients	NO	NO	NO	Used in epidurals	NO	NO	NO	Visual Analogue Scale
Sedation hold strategy	No consistency in sedation hold practice. Sedation hold performed as part of VAP bundle. Gradual reduction of sedation. Not protocolized.	Done at 8am daily as part of VAP bundle.	No consistency in sedation hold practice. Individualised approach. Sedation hold performed as part of VAP bundle.	Individualised approach to sedation hold. Not protocolized. Sedation hold performed as part of VAP bundle.	Individualised approach to sedation hold. Not protocolized. Sedation hold performed as part of VAP bundle.	Individualised approach to sedation hold. Not protocolized. Sedation hold performed as part of VAP bundle.	Individualised approach to sedation hold. Sedation hold protocol available.	Individualised approach to sedation hold. Not protocolized. Sedation hold performed as part of VAP bundle.

Table S2: Detailed breakdown of the diagnostic categories of the patients enrolled in the study at each ICU during each study period. All values are N (%).

		Education		Education + Process Feedback		Education + Responsiveness Monitoring		Education + Process Feedback + Responsiveness Monitoring	
Diagnostic Category	**Study Period**	**ICU1**	**ICU2**	**ICU3**	**ICU4**	**ICU5**	**ICU6**	**ICU7**	**ICU8**
Cardiovascular	Baseline	38 (32·2%)	29 (29·6%)	83 (35·2%)	34 (33·3%)	30 (28·0%)	15 (24·6%)	18 (20·7%)	12 (16·7%)
	Intervention	20 (30·8%)	16 (27·6%)	60 (35·7%)	25 (46·3%)	9 (14·5%)	7 (25·0%)	18 (16·4%)	8 (18·6%)
Respiratory	Baseline	34 (28·8%)	39 (39·8%)	46 (19·5%)	32 (31·4%)	32 (29·9%)	26 (42·6%)	25 (28·7%)	32 (44·4%)
	Intervention	16 (24·6%)	12 (20·7%)	31 (18·5%)	8 (14·8%)	24 (38·7%)	15 (53·6%)	36 (32·7%)	16 (37·2%)
Gastrointestinal	Baseline	17 (14·4%)	15 (15·3%)	73 (30·9%)	11 (10·8%)	26 (24·3%)	11 (18·0%)	24 (27·6%)	14 (19·4%)
	Intervention	15 (23·1%)	13 (22·4%)	54 (32·1%)	10 (18·5%)	20 (32·3%)	5 (17·9%)	24 (21·8%)	11 (25·6%)
Trauma	Baseline	6 (5·1%)	0 (0·0%)	4 (1·7%)	12 (11·8%)	4 (3·7%)	0 (0·0%)	4 (4·6%)	2 (2·8%)
	Intervention	2 (3·1%)	0 (0·0%)	10 (6·0%)	4 (7·4%)	1 (1·6%)	0 (0·0%)	8 (7·3%)	1 (2·3%)
Neurological	Baseline	10 (8·5%)	6 (6·1%)	12 (5·1%)	7 (6·9%)	7 (6·5%)	1 (1·6%)	10 (11·5%)	4 (5·6%)
	Intervention	3 (4·6%)	6 (10·3%)	4 (2·4%)	4 (7·4%)	1 (1·6%)	0 (0·0%)	11 (10·0%)	3 (7·0%)
Obstetrics	Baseline	0 (0·0%)	1 (1·0%)	0 (0·0%)	0 (0·0%)	0 (0·0%)	0 (0·0%)	1 (1·1%)	0 (0·0%)
	Intervention	0 (0·0%)	0 (0·0%)	1 (0·6%)	0 (0·0%)	0 (0·0%)	0 (0·0%)	1 (0·9%)	0 (0·0%)
Self-Inflicted Overdose	Baseline	4 (3·4%)	2 (2·0%)	8 (3·4%)	2 (2·0%)	3 (2·8%)	6 (9·8%)	1 (1·1%)	2 (2·8%)
	Intervention	4 (6·2%)	3 (5·2%)	4 (2·4%)	2 (3·7%)	2 (3·2%)	1 (3·6%)	2 (1·8%)	1 (2·3%)
Miscellaneous Diagnoses	Baseline	7 (5·9%)	4 (4·1%)	8 (3·4%)	4 (3·9%)	5 (4·7%)	1 (1·6%)	4 (4·6%)	2 (2·8%)
	Intervention	3 (4·6%)	5 (8·6%)	4 (2·4%)	1 (1·9%)	1 (1·6%)	0 (0·0%)	7 (6·4%)	2 (4·7%)

Renal Diagnosis	Baseline	2 (1·7%)	2 (2·0%)	2 (0·8%)	0 (0·0%)	0 (0·0%)	1 (1·6%)	0 (0·0%)	4 (5·6%)
	Intervention	2 (3·1%)	3 (5·2%)	0 (0·0%)	0 (0·0%)	4 (6·5%)	0 (0·0%)	3 (2·7%)	1 (2·3%)

Table S3: Detailed summary of the numbers of patients in screening and inclusion processes for each ICU during the baseline and intervention periods.

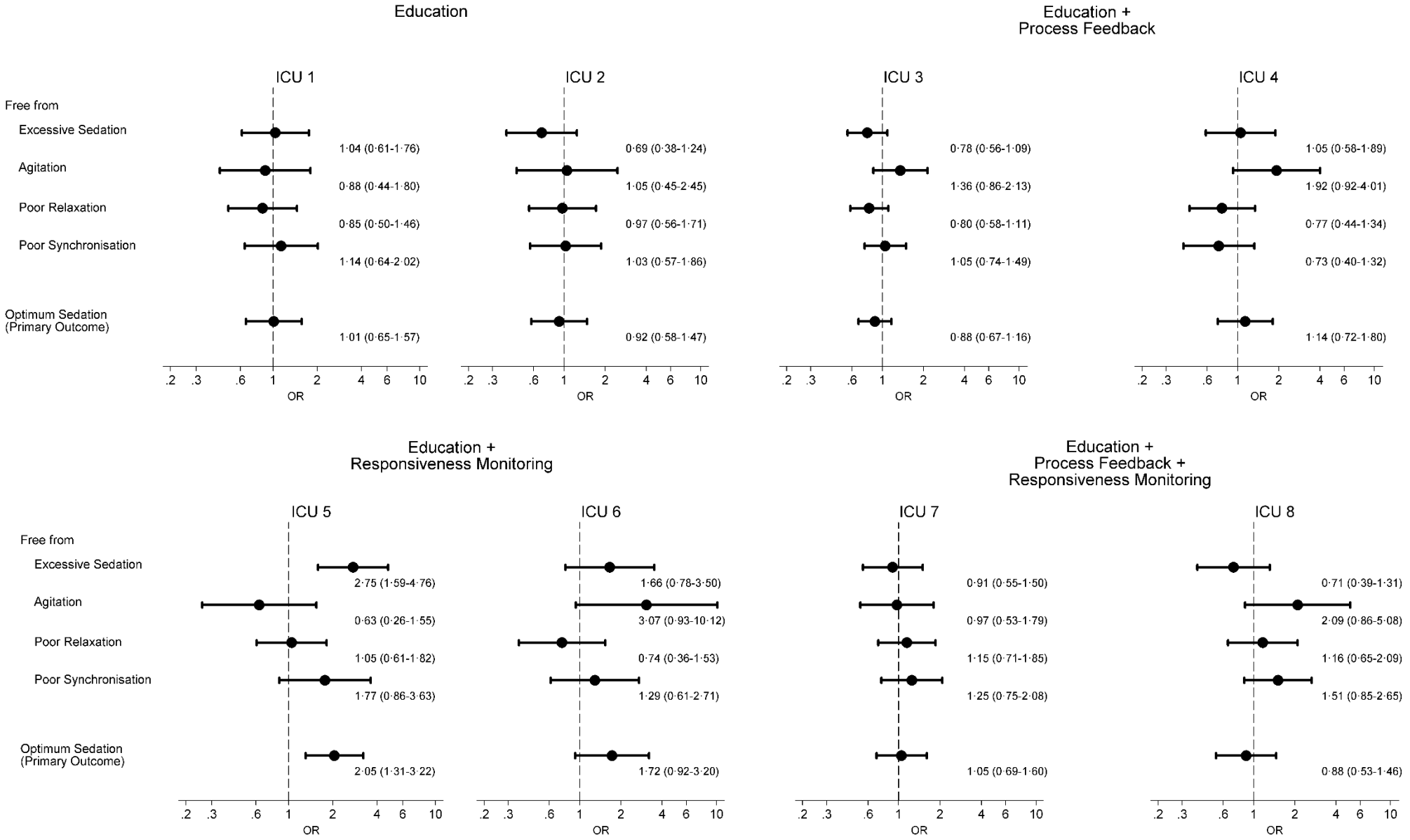
		Education		Education + Process Feedback		Education + Responsiveness Monitoring		Education + Process Feedback + Responsiveness Monitoring	
		ICU 1	ICU2	ICU3	ICU4	ICU5	ICU6	ICU7	ICU8
BASELINE PERIOD (45 WEEKS)	SCREENED (N)	1225	483	1015	408	374	282	722	315
	EXCLUDED	1019	293	562	134	239	141	499	209
	Died	17	23	30	10	8	16	3	5
	Age <16 years	13	3	5	8	11	2	4	0
	For palliative care	8	1	1	1	0	1	2	1
	No mechanical ventilation	894	162	272	27	153	55	343	54
	Mechanical ventilation discontinued at time of screening	49	67	139	33	31	36	109	33
	Extubation anticipated within 4 hours of screening	19	28	73	34	26	22	25	84
	Decision made to withdraw treatment	14	1	15	18	10	6	9	31
	Already enrolled in the study during current hospital admission	5	8	27	3	0	3	4	1
	ELIGIBLE	206	190	453	274	135	141	223	106
	CONSENTED (% of eligible patients)	120 (58)	98 (52)	236 (52)	103 (38)	108 (80)	61 (43)	92 (41)	74 (70)
	Reason not consented								
	No one available to provide consent	17	31	34	24	3	6	48	10
	Lack of research staff	3	0	32	47	0	5	1	0
	Not approached	21	1	37	19	10	23	24	6
	Clinician refusal	2	24	18	8	0	2	9	6

	Consent not obtained within 48 hours of admission	32	22	79	44	4	27	35	6
	Other	11	14	17	29	10	17	14	4
	EXCLUDED FROM ALL ANALYSES (status epilepticus)	2	0	0	1	1	0	5	2
	PRIMARY OUTCOME DATA AVAILABLE	113	91	232	101	104	61	78	67
	Reason for no primary outcome data								
	Mechanical ventilation for <48 hours	3	5	4	0	3	0	7	4
	Receiving neuromuscular paralysis	2	1	0	0	0	0	0	1
	No SQATs completed	0	1	0	1	0	0	2	0
		Education		**Education + Process Feedback**		**Education + Responsiveness Monitoring**		**Education + Process Feedback + Responsiveness Monitoring**	
		ICU 1	**ICU2**	**ICU3**	**ICU4**	**ICU5**	**ICU6**	**ICU7**	**ICU8**
INTERVENTION PERIOD (45 WEEKS)	SCREENED (N)	1105	369	944	345	244	191	394	209
	EXCLUDED	987	249	638	182	154	110	193	146
	Died	27	23	18	23	3	17	4	0
	Age <16 years	8	3	2	2	4	0	2	0
	For palliative care	6	0	1	0	0	0	2	0
	No mechanical ventilation	866	123	302	33	102	28	84	48
	Mechanical ventilation discontinued at time of screening	37	54	178	74	33	42	55	50
	Extubation anticipated within 4 hours of screening	42	29	112	31	11	21	33	30
	Decision made to withdraw treatment	0	13	22	15	1	2	10	11

	Already enrolled in the study during current hospital admission	1	4	3	4	0	0	3	7
	ELIGIBLE	118	120	306	163	90	81	201	63
	CONSENTED (% of eligible patients)	65 (55)	58 (48)	170 (56)	55 (34)	62 (69)	28 (35)	116 (58)	44 (70)
	Reason not consented								
	No one available to provide consent	6	11	25	8	2	11	10	2
	Lack of research staff	4	6	6	17	0	0	4	0
	Not approached	2	9	13	46	3	4	8	1
	Clinician refusal	0	17	10	3	0	1	1	0
	Consent not obtained within 48 hours of admission	23	5	25	5	1	31	26	0
	Other	18	14	57	29	22	6	36	16
	EXCLUDED FROM ALL ANALYSES (status epilepticus)	0	0	2	1	0	0	4	0
	PRIMARY OUTCOME DATA AVAILABLE	64	56	167	52	61	28	107	42
	Reason for no primary outcome data								
	Mechanical ventilation for <48 hours	1	1	1	1	1	0	4	0
	Receiving neuromuscular paralysis	0	0	0	0	0	0	1	2
	No SQATs completed	0	1	0	1	0	0	0	0

Note: SQAT, sedation quality assessment tool.

Figure S1: Estimates of joint effects of interventions, odds ratios (OR) and 95% confidence intervals, in each ICU on sedation-analgesia quality measures at DESIST care period level from modelling, prior to pooled analysis. An OR >1 indicates an increase in outcome with the intervention(s) (improvement).



Note: Results are from a generalised linear model with logit link. Adjusted for age, sex and APACHE II score.

Table S4: Number of patients and number of care periods with data available on primary outcome (optimum sedation-analgesia), and number of care periods with optimum sedation-analgesia by intervention group and study period. All data presented are raw data before modelling.

	Baseline period			**Intervention period**		
Intervention	Patients (N)	Care periods (N)	Care periods with optimum sedation (N (%))	Patients (N)	Care periods (N)	Care periods with optimum sedation (N (%))
Education	847	9187	5150 (56·1)	577	6947	3940 (56·7)
Process Feedback						
Implemented	478	5383	2930 (54·4)	368	4725	2526 (53·5)
Not Implemented	369	3804	2220 (58·4)	209	2222	1414 (63·6)
Responsiveness Monitoring						
Implemented	310	2902	1486 (51·2)	238	2858	1663 (58·2)
Not Implemented	537	6285	3664 (58·3)	339	4089	2277 (55·7)

Note: There were 42 and 15 patients from the baseline and intervention periods respectively for whom the APACHE II score was imputed. Only 1 and 3 patients from the baseline and intervention periods respectively were excluded from statistical modelling due to missing covariate(s).

Table S5: Intraclass correlation coefficients (ICCs) for the primary outcome and the two-level secondary outcomes.

Outcome	**ICC**
Sedation-Analgesia Quality Measures at Care Period Level	
Primary Outcome	
Optimum Sedation	0·25
Components of Primary Outcome	
Free from Excessive Sedation	0·34
Free from Agitation	0·40
Free from Poor Relaxation	0·29
Free from Poor Synchronisation	0·27
Sedation-Related Adverse Events	
Day on which a Sedation-Related Adverse Event (SRAE) occurred	0·21
Sedative and Analgesic Drug Use	
Day on which ≥4000mg Propofol (or equivalents) administered	0·60

Table S6: Sensitivity analyses exploring effects of each intervention based on those patients enrolled during final 30 weeks of the intervention period.

Table S6(a): Estimates of effects on sedation-analgesia quality measures at DESIST care period level. An odds ratio (OR) >1 indicates an increase in the outcome with the intervention (improvement).

		Education	**Process Feedback**	**Responsiveness Monitoring**
Primary Outcome				
Optimum Sedation	OR (95% CI)	1·14 (0·83-1·57)	**0·66 (0·46-0·94)**	**1·51 (1·06-2·16)**
Components of Primary Outcome				
Free from Excessive Sedation	OR (95% CI)	1·12 (0·75-1·65)	**0·57 (0·36-0·89)**	**1·55 (1·00-2·38)**
Free from Agitation	OR (95% CI)	1·27 (0·71-2·26)	1·01 (0·53-1·94)	0·83 (0·46-1·50)
Free from Poor Relaxation	OR (95% CI)	0·77 (0·52-1·13)	0·96 (0·63-1·46)	1·35 (0·89-2·05)
Free from Poor Synchronisation	OR (95% CI)	1·23 (0·83-1·83)	0·78 (0·49-1·24)	**1·84 (1·19-2·85)**

Note: Outcomes with statistically significant intervention effects (95% confidence intervals (CIs) do not overlap 1) are highlighted in bold. Results are from multilevel generalised linear model with logit link. Adjusted for age, sex and APACHE II score.

Table S6(b): Estimates of effects on sedation-analgesia quality measures at patient level. A rate ratio (RR) >1 indicates an increase in the outcome with the intervention (improvement).

		Education	**Process Feedback**	**Responsiveness Monitoring**
Optimum Sedation	RR (95% CI)	1·03 (0·92-1·15)	**0·86 (0·75-0·98)**	**1·17 (1·02-1·35)**
Free from Excessive Sedation	RR (95% CI)	1·02 (0·95-1·10)	**0·88 (0·81-0·96)**	1·07 (0·98-1·16)
Free from Agitation	RR (95% CI)	1·02 (0·96-1·09)	1·02 (0·94-1·10)	0·97 (0·90-1·05)
Free from Poor Relaxation	RR (95% CI)	0·97 (0·91-1·04)	0·97 (0·89-1·05)	1·05 (0·96-1·14)
Free from Poor Synchronisation	RR (95% CI)	1·02 (0·95-1·09)	0·98 (0·90-1·06)	1·05 (0·97-1·14)

Note: Outcomes with statistically significant intervention effects (95% confidence intervals (CIs) do not overlap 1) are highlighted in bold. Results are from generalised linear model with log link and negative binomial error distribution for number of DESIST care periods with an outcomes present for each patient, using the total number of DESIST care periods with valid data for that outcome for each patient as an offset. Adjusted for age, sex and APACHE II score.

Table S6(c): Estimates of effects on sedation related adverse event (SRAE) outcomes. An odds ratio (OR) <1 indicates a decrease in the outcome with intervention (improvement).

		Education	**Process Feedback**	**Responsiveness Monitoring**
Day on which a SRAE Occurred	OR (95% CI)	0·61 (0·33-1·13)	0·85 (0·42-1·72)	**2·23 (1·09-4·57)**
Patient Experienced a SRAE	OR (95% CI)	0·55 (0·30-1·04)	1·04 (0·52-2·08)	**2·54 (1·25-5·15)**

Note: Outcomes with statistically significant intervention effects (95% confidence intervals (CIs) do not overlap 1) are highlighted in bold. Results are from multilevel generalised linear model with logit link for SRAE at day level and a generalised linear model with logit link for SRAE at patient level. Adjusted for age, sex and APACHE II score.

CHANGES TO ORIGINAL ANALYSIS PLAN

In analysing the four components (excessive sedation; agitation; poor relaxation; poor ventilator synchronisation) of optimum sedation-analgesia we inverted these to model at care period level those which were free from excessive sedation, free from agitation, free from poor relaxation and free from poor ventilator synchronisation, and at patient level the number of care periods free from excessive sedation, free from agitation, free from poor relaxation and free from poor ventilator synchronisation. This clarified the presentation of the analysis by ensuring that an odds ratio or rate ratio >1 represented a favourable effect for both optimum sedation and each of the four components. [Figure 2, Tables 2A, S6(a), S6(b)]

For the analysis of optimum sedation and its components at patient level, we used a generalised linear model with log link but a negative binomial rather than the Poisson error distribution that was originally planned. This accounted appropriately for the unexpected over-dispersion observed in these outcomes. [Tables 2A, S6(b)]

PROCESS EVALUATION

Aim

A key goal of the process evaluation was to understand whether the interventions were implemented as planned, the barriers to implementation, and factors that worked well/less well. We planned a priori to compare effects between ICUs in which successful engagement and implementation appeared to occur versus those with less successful engagement and implementation. The cluster randomised design of DESIST allowed this comparison. The analysis strategy was a mixed methods approach in which qualitative data were used to provide context and explanation of the quantitative findings.

Education intervention

A total of 538 nurses completed the training. The eight ICUs achieved 74%, 80%, 80%, 96%, 96%, 98%, 100%, and 100% training completion of eligible nursing staff. The mean pre-training core knowledge test score (range 0-10) was 6.4 (SD 1.8). In total 394 nurses (73%) completed the re-test a median 32 weeks (1^{st}-3^{rd} quartile 28-39 weeks) after first test. The mean change in scores, adjusted for pre-test score, showed an increase of 0.82 (95% CI: 0.65-0.98; P<0.0001).

Responsiveness monitoring

In the four ICUs a total of 206 patients received RI monitoring (82% enrolled patients; range 76% to 95% between ICUs). The median (1st, 3rd quartile) time between intubation and starting monitoring was 21 hours (11, 34) and median duration of monitoring was 66 hours (27, 139). The first RI recorded was: red 59% (range 50-66% across ICUs), amber 12% (range 4-17%), and green 28% (range 25-38%). Among patients whose first RI was red 16% never had a green RI of whom 68% were ICU non-survivors. The median time to first recording a green RI when this occurred was 9 hours (4, 23). Among all patients the RI value was red for a median 35% of monitored time (range 23-48% across ICUs); the median longest recorded time with continuous red RI values within each patient was 7 hours (3, 14). Together these data suggested significant periods of low RI values despite the instruction to adjust sedation to achieve a higher RI value in the amber or green range.

Qualitative evaluation

Qualitative data were collected both during the baseline, during the implementation phase, and during the intervention periods of the study. We conducted multi-professional focus groups in each ICU prior to the implementation phase to understand the current culture of sedation practice.

During the implementation period and intervention phase action research involving participant observation took place at each ICU at three distinct times to understand the uptake of the interventions and changes in practice: the end of implementation phase, midway during the intervention period, and at the end of the intervention period. We conducted multi-professional focus groups in the final month of the intervention period, in which participants reflected on the uptake of the intervention(s) and the changes to sedation practice. Data from field notes from participant observation and focus groups transcripts were verbatim transcribed and then checked for accuracy of transcription by the qualitative researcher (KK). Data were entered in NVivo 10 for windows software for qualitative analysis (QSR International, Ltd).

Data were organised by ICU setting for coding. An inductive thematic analysis was conducted without a pre-defined theoretical framework to allow the in-depth exploration and understanding of the impact of interventions on sedation management. Constant comparison ensured that the thematic analysis represented all perspectives and negative cases were sought. Validity checking of the coding included recoding of data from 4 ICUs, representative of each intervention group, by an independent researcher (GH). Discordant coding and agreement was resolved by discussion within the wider research team.

Data were extracted in relation to the characteristics of the interventions, its compatibility with the clinicians, its visibility in the clinical environment, any compelling attributes and the timing the intervention was introduced. Data related to the dissemination and the adoption of the intervention(s) included the adopters' intra-individual factors such as their expectations of the intervention(s), the meaning of the intervention to them, their learning style and their tolerance of ambiguity about the intervention. Elements of the clinicians' communication channels, availability of linkage agents, their clinical routines and existing cultures (such as documentation processes, daily housekeeping processes), elements of the ICU environment (size, facilities), geography of the setting (floor plan, types of admissions due to the geographical area) informed the adoption of the interventions. Clinicians' initial expectations of the interventions as well as their knowledge of the intervention, including awareness knowledge (that the innovation exists), procedural knowledge (how to use the intervention) and principles knowledge (how the intervention works) were considered. Although some strategies to implement the interventions were suggested, we recorded how clinicians adjusted these strategies to facilitate implementation of interventions. We recorded the barriers and facilitators to implementation and adoption, and the role of staff involvement, including leadership roles, teamwork elements, and communication channels. In this supplement we present the clinicians' perceived feedback on the use of the three interventions and the response of

each ICU to the implementation of the interventions including any changes observed in their sedation-analgesia practice (Tables S7 and S8).

Table S7: Clinicians' feedback on each intervention.

Education		**Process Feedback**		**Responsiveness Monitoring**	
Positive comments	**Negative comments**	**Positive comments**	**Negative comments**	**Positive comments**	**Negative comments**
Informative and useful, in particular for junior staff. For senior nurses was a good reminder. Met educational needs of staff. Had a good summative assessment. Staff were familiar with the online platform used (LearnPro).	Time consuming. Overwhelming for some junior staff. Some technical problems with access to the module delayed implementation (3 ICUs). Debatable format (e-form vs hard copies). Nurses needed feedback on the online assessments of knowledge.	Stimulated discussion about suboptimum sedation. Used existing QI methodology and presentation familiar to the staff.	Disbelief in how the process measures were derived. Nurses felt SQAT tool questions, from which the process measures were derived, were not relevant to some patient cases and did not reflect current practice. (i.e. felt agitation was more prevalent to excessive sedation). Process measures were not meaningful to nurses. Lack of understanding of the charts by the nurses. The process measures were not disseminated timely; they needed to be presented weekly to drive change. No consistent presentation. The style of presentation needed improvement.	Monitor was easy to use and was a good prompt tool for some patient cases. Families found it useful. Used mainly as a research tool.	Lack of understanding of the role of the monitor. Some nurses felt it was useless. There was no correlation of the monitor with the clinical picture in certain patients. Created disbelief. There was time lag between monitor recording and physical presentation of the patient. Non adhesive stickers - increased gaps in recording. Skin excoriation because of the stickers. Big size was a problem for small ICUs. Some faulty parts of the monitor. Families found it invasive.

Table S8: Perceived changes in sedation-analgesia practice due to each intervention.

Education	**Process Feedback**	**Responsiveness Monitoring**
Raised awareness of sedation-analgesia management, sleep promotion, drug properties, delirium and agitation, psychosis. Able to differentiate between sedation and analgesia management. Nurses felt more confident in their decision-making. Introduced sleep promotion initiatives. Re-enforced the use of sedation breaks and reviewing their timing. Introduced new tools for assessment of pain (CPOT), delirium (CAM-ICU), and sedation, where not available. Introduced/ updated protocols for management of sedation, agitation, delirium and pain. Considered introducing agents for managing psychosis and delirium.	Recognised the need for improvement of sedation-analgesia practice. Recognised the need for a standardised manner in managing sedation-analgesia. Raised awareness of suboptimum sedation practice. Introduced/ updated daily review of sedation-analgesia management and documentation where not available or not consistently performed. Introduced checklists (e.g. ICU pause) in ward round meetings or safety briefs as an aide-memoir tool to highlight sedation-analgesia issues regularly. Introduced audits on use of assessment tools, sleep quality, and pain.	Used as a prompt tool to identify excessive sedation and detect sleep. Able to differentiate between sleep and sedation. Informed decisions about excessive sedation. Reviewed the use of sedation boluses as a management method for agitation, observing their effect on the monitor recording and the physical appearance of the patient. Identified the need to introduce a sleep promotion protocol.

Example of a full set of process feedback for one of the ICUs randomised to receive process feedback during the study

SEDATION RELATED QUALITY MEASURES REPORT – 21st DECEMBER 2014

Background

The DESIST study is evaluating different approaches to improving the quality of sedation of intensive care patients. One of the approaches is to provide feedback on a range of quality indicators. This report provides you with information about the prevalence of excessive sedation, agitation, discomfort and sedation-related adverse events in your ICU. It also provides an overall measure of optimum sedation among patients.

The information used to generate these reports was recorded by nursing staff using the Sedation Quality Assessment Tool (SQAT) forms for each nursing shift, and information collected by research staff for the DESIST study.

How to use these reports

The information included in this report is intended to help improve sedation management in your ICU by providing you with feedback on current sedation quality. We suggest that information is shared with all staff groups through a range of media such as e-mail, posters, quality briefs, and meetings. We suggest that reports are reviewed at medical and nursing staff meetings, quality improvement teams, M&M meetings, and/or other local meetings in your ICU. We also encourage you to disseminate the findings in daily practice, for example at handovers or ward rounds. We hope you will use the information to review current sedation management, and initiate interventions and changes that will improve all aspects of sedation management. These charts will help you to monitor the effect of your interventions and changes.

The reports have been designed to illustrate changes over time, especially improvements or deterioration in performance for each quality measure. Reports will be circulated every 2 months, using recently collected data from the DESIST study. In this way the impact of local initiatives to improve management can be seen. We hope you will supplement these with local data collected more frequently; we have provided you with "toolkits" to do this.

Summary Points

This is the final process measures report for the intervention period of DESIST. The report includes data from all patient cases entered to the database during the intervention period with resolved queries. It presents the last 2 months of recruitment.

In October to November 2014:

Proportion during October – November 2014	**Proportion during August – September 2014**	**Effect on sedation quality**
Excessive sedation was present for **26%** of care periods	**16%**	10% **HIGHER** rate of excessive sedation 
Agitation was present for **7%** of care periods	**11%**	4% **LOWER** rate of agitation 
Poor relaxation (a measure of pain and discomfort) was present for **12%** of care periods	**19.5%**	7.5% **LOWER** rate of poor relaxation 
Poor ventilator synchronisation was present for **5%** of care periods	**8.5%**	3.5% **LOWER** rate of poor ventilator synchronisation 
4 sedation-related adverse events occurred during this period	**9**	**FEWER** sedation-related adverse events 
Overall, optimum sedation was present for 62% of care periods	**61%**	1% **HIGHER** rate of optimum sedation 

Understanding the charts

This report includes a series of *process control* charts, each under a separate section. Each chart includes:

1. A summary of how the quality indicator has been calculated from your data.
2. A **baseline proportion**. Depending on the type of chart, this is the average value for the quality indicator during your baseline "pre-intervention" period (the data collected during the first 11 months of the DESIST study, from October 2012 to August 2013).
3. **Process "warning" and "control" limits**. These upper and lower limits are calculated to assess whether the rate of the quality indicator has changed significantly in your ICU. If a warning limit is exceeded it means the quality indicator is in danger of moving "out of control" compared to the baseline rate. This could be good or bad depending on the direction of change. If a control limit is crossed, this probably means there has been a "real" change in the measure compared to the baseline rate. This might indicate a significant improvement or deterioration in the measure according to the direction of change.
4. **Data points**. A data point is included for every 2 months throughout the pre-intervention (baseline) and post-intervention periods for most charts. Each data point uses the available data from patients enrolled in the DESIST study for that period.

Charts

The following charts are included in this report:

P charts: these charts show the proportion of nursing shifts (12 hour periods) for which the quality indicator was reported.

- Proportion of periods with excessive sedation
- Proportion of periods with agitation
- Proportion of periods for which patient poorly relaxed
- Proportion of periods with poor ventilator synchronisation
- Proportion of periods with optimum sedation

G charts: these charts show the number of patients managed between the quality indicator events occurring.

- Number of patients treated without a sedation-related adverse event

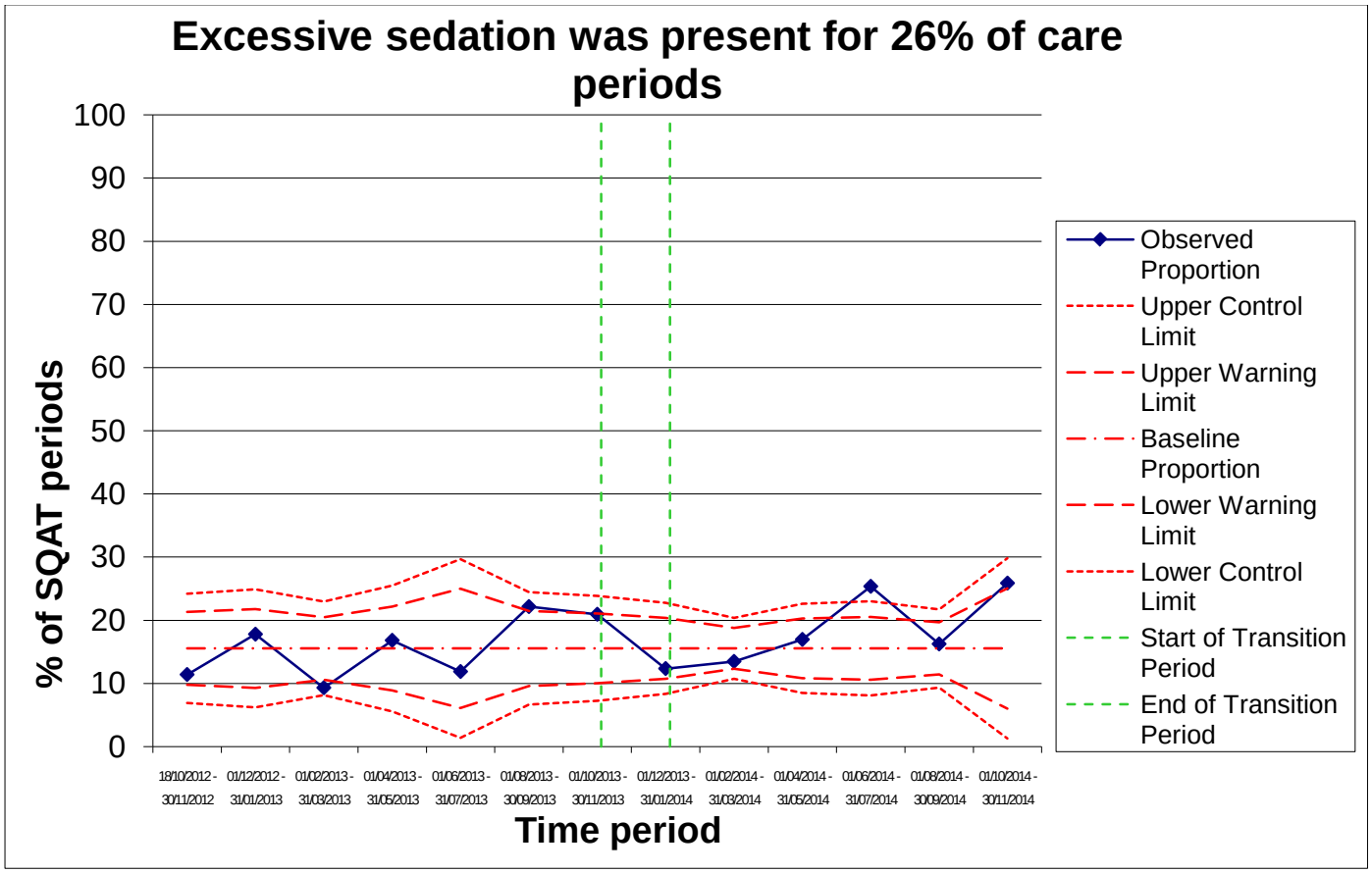
Sedation-related adverse events

- Frequency table of all sedation related adverse events recorded during this period

"Proportion of periods with excessive sedation"

How was this chart made?

The data recorded by nurses on the SQAT form at the end of each shift was used to count the number of periods for which deep sedation was present. Information included on the SQAT form was used to exclude periods where deep sedation may have been appropriate, for example advanced ventilation, therapeutic hypothermia, or brain injury. The remaining periods were considered excessive sedation, because evidence would suggest these patients benefit from "lighter" sedation. Each data point has used 2 months of ICU admissions participating in the DESIST study.



What does this chart mean?

The **proportion** is the average rate of this quality measure that occurred in your ICU during the intervention period October to November 2014 in the DESIST study. **This means that for 26% of care periods in the ICU excessive sedation was present using the DESIST definition.**

The **observed proportion** is the rate of excessive sedation over 2 months of observations in the ICU. If the proportion moves closer to the **upper warning or control limit**, the occurrence of excessive sedation is *increasing*. If it crosses the **upper control limit** this represents a significant increase in excessive sedation in your ICU. If the proportion moves closer to the **lower warning or control limit**, the occurrence of excessive sedation is *decreasing*. If it crosses the **lower control limit** this represents a significant decrease in excessive sedation in your ICU.

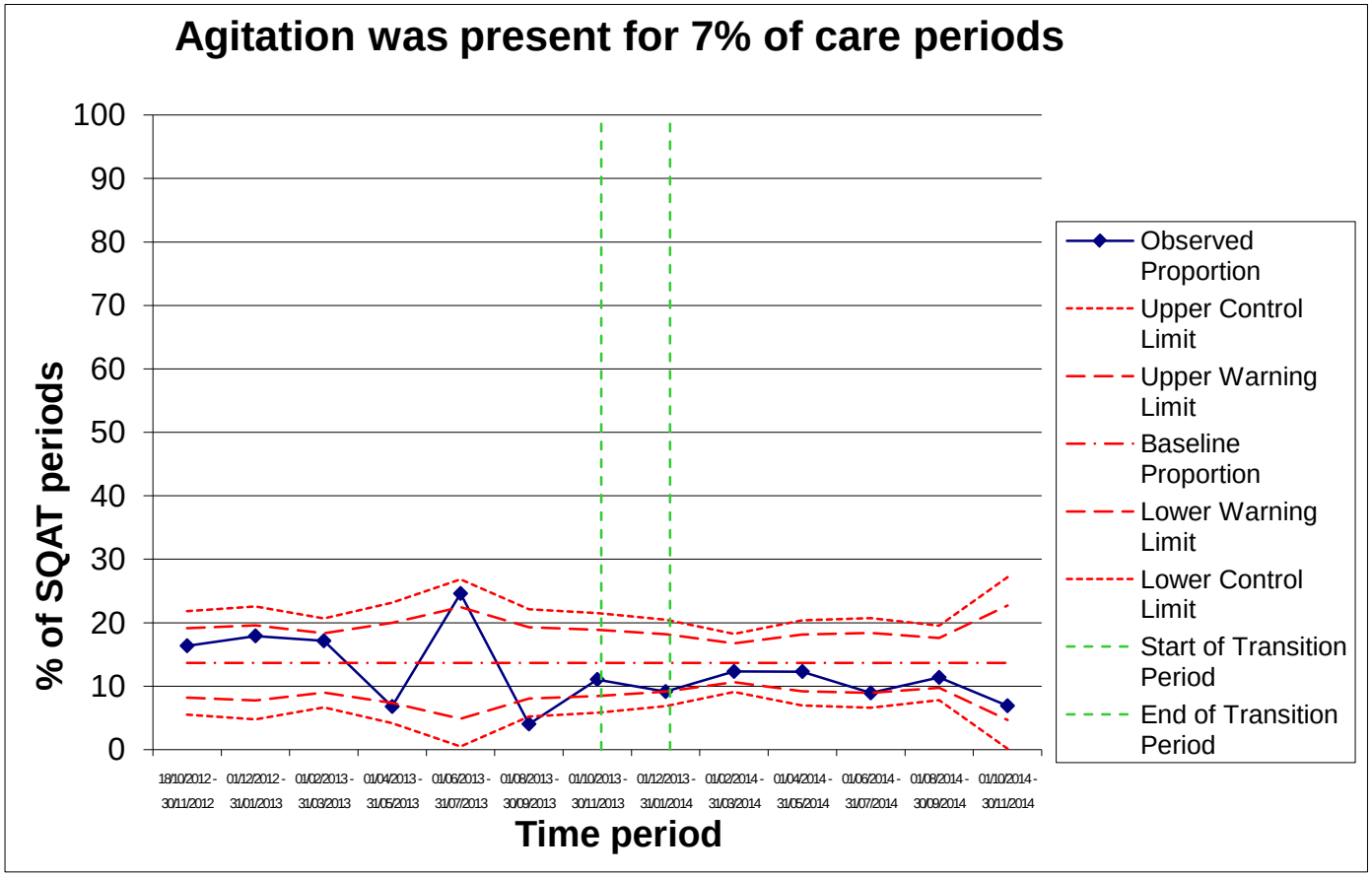
This chart suggests there has been INCREASE in excessive sedation during the period October to November 2014.

To learn more about the importance of excessive sedation and how to avoid it, access the DESIST LearnPro education package, modules 1 (*Why is it important to get sedation right?)* and 4 (*avoiding excessive sedation*).

"Proportion of periods with agitation"

How was this chart made?

The data recorded by nurses on the SQAT form at the end of each shift was used to count the number of periods for which agitation was present. Each data point has used 2 months of ICU admissions participating in the DESIST study.



What does this chart mean?

The **proportion** is the average rate of this quality measure that occurred in the ICU during the intervention period October to November 2014 in the DESIST study. **This means that for 7% of care periods in the ICU agitation was present using the DESIST definition.**

The **observed proportion** is the rate of agitation over 2 months of observations in the ICU. If the proportion moves closer to the **upper warning or control limit**, the occurrence of agitation is increasing. If it crosses the

upper control limit this represents a significant increase in agitation in your ICU. If the proportion moves closer to the **lower warning or control limit**, the occurrence of agitation is decreasing. If it crosses the **lower control limit** this represents a significant decrease in agitation in your ICU.

This chart suggests there has been DECREASE in agitation during the period October to November 2014.

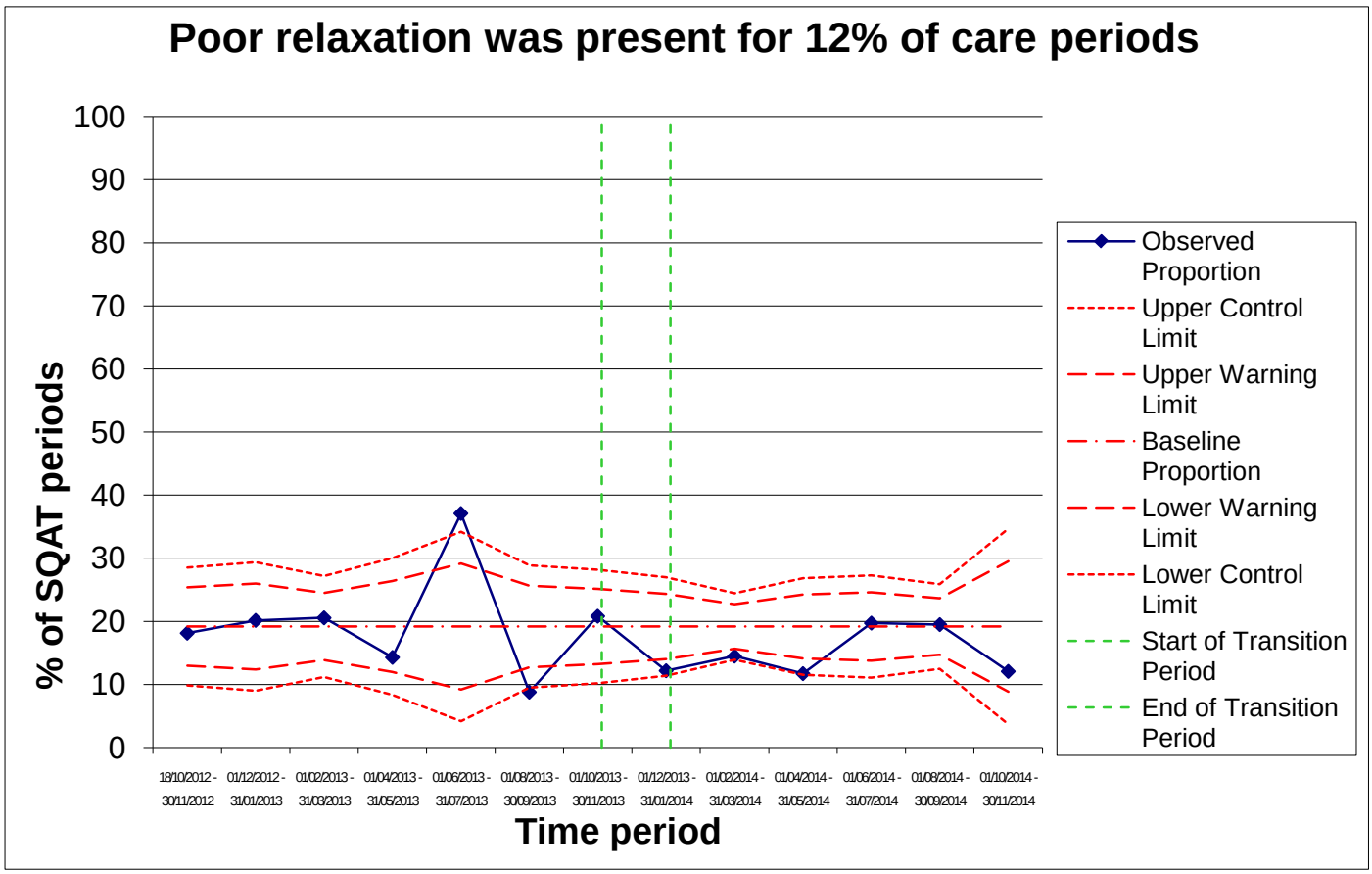
Agitation has several causes, including pain, poor ventilator synchronisation, delirium, anxiety, drug withdrawal syndromes, or other causes of discomfort such as bowel discomfort (eg. constipation/distension).

To learn more about managing agitation, access the DESIST LearnPro education package, modules 6 (*managing agitation*), 7 (*managing delirium*), and 8 (*drug withdrawal*).

"Proportion of periods during which patient poorly relaxed"

How was this chart made?

The data recorded by nurses on the SQAT form at the end of each shift was used to count the number of periods for which patients were poorly relaxed based on ease of movement. Each data point has used 2 months of ICU admissions participating in the DESIST study.



What does this chart mean?

Poor relaxation is probably the best way of assessing pain and discomfort in patients unable to communicate verbally during critical illness.

The **proportion** is the average rate of this quality measure that occurred in the ICU during the intervention period October to November 2014 in the DESIST study. **This means that for 12% of care periods in the ICU poor relaxation was present using the DESIST definition.**

The **observed proportion** is the rate of poor relaxation over 2 months of observations in the ICU. If the proportion moves closer to the **upper warning or control limit**, the occurrence of poor relaxation is increasing. If it crosses the **upper control limit** this represents a significant increase in poor relaxation in your ICU. If the proportion moves closer to the **lower warning or control limit**, the occurrence of poor relaxation is decreasing. If it crosses the **lower control limit** this represents a significant decrease in poor relaxation in your ICU.

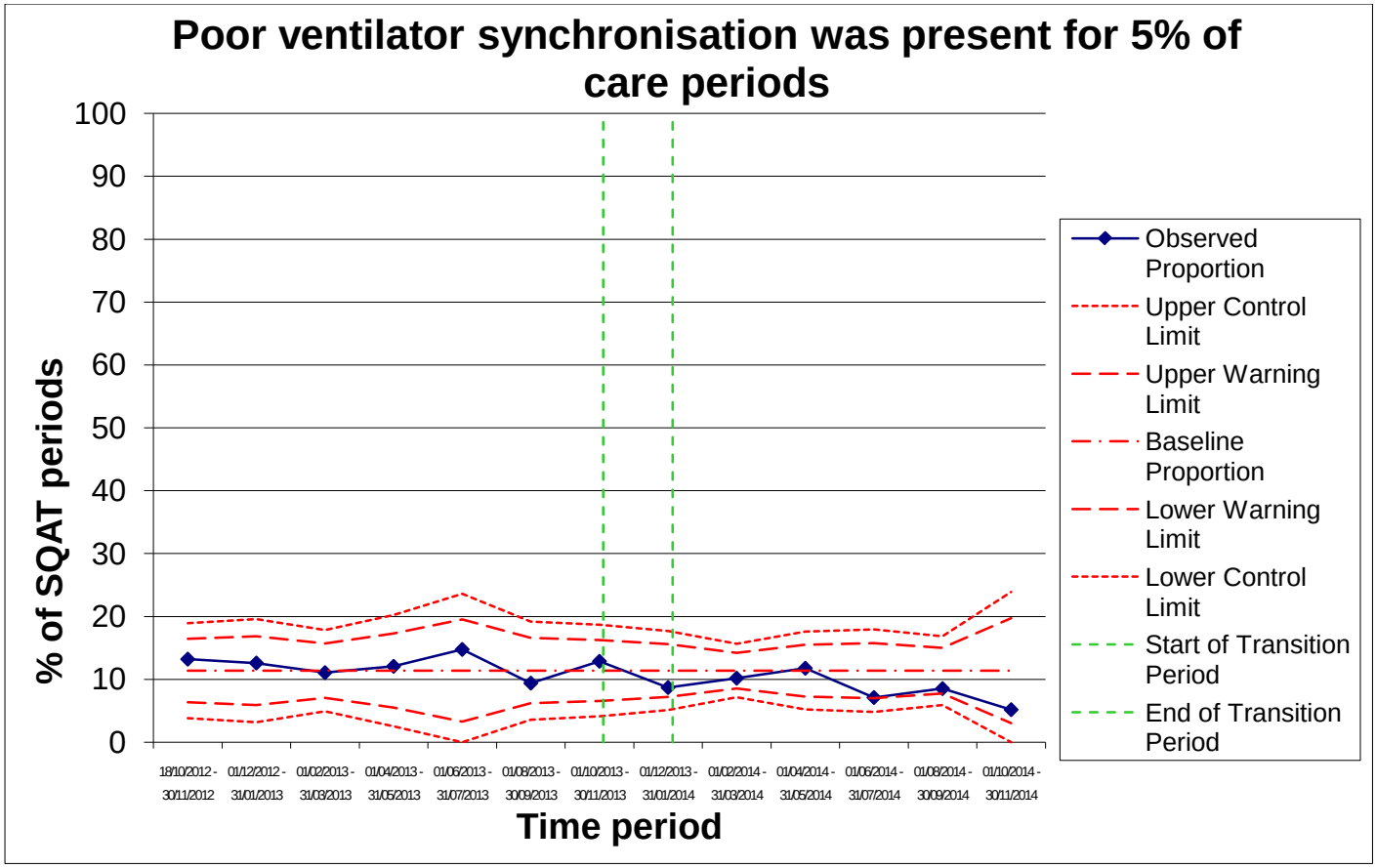
This chart suggests that there has been DECREASE in poor relaxation (pain/discomfort) during the period October to November 2014.

To learn more about managing pain access the DESIST LearnPro education package, module 5 (*assessing pain and discomfort in ICU*).

"Proportion of periods with poor ventilator synchronisation"

How was this chart made?

The data recorded by nurses on the SQAT form at the end of each shift was used to count the number of periods for which patients had poor ventilator synchronisation (coughing or gagging frequently or unable to control ventilation despite adjustments). Each data point has used 2 months of ICU admissions participating in the DESIST study.



What does this chart mean?

The **proportion** is the average rate of this quality measure that occurred in the the ICU during the intervention period October to November 2014 in the DESIST study. **This means that for 5% of care periods in the ICU poor ventilator synchronisation was present using the DESIST definition.**

The **observed proportion** is the rate of poor ventilator synchronisation over 2 months of observations in the the ICU. If the proportion moves closer to the **upper warning or control limit**, the occurrence of poor ventilator synchronisation is increasing. If it crosses the **upper control limit** this represents a significant increase in poor ventilator synchronisation in your ICU. If the proportion moves closer to the **lower warning or control limit**, the occurrence of poor ventilator synchronisation is decreasing. If it crosses the **lower control limit** this represents a significant decrease in poor ventilator synchronisation in your ICU.

This chart suggests there has been DECREASE in poor ventilator synchronisation during the period October to November 2014.

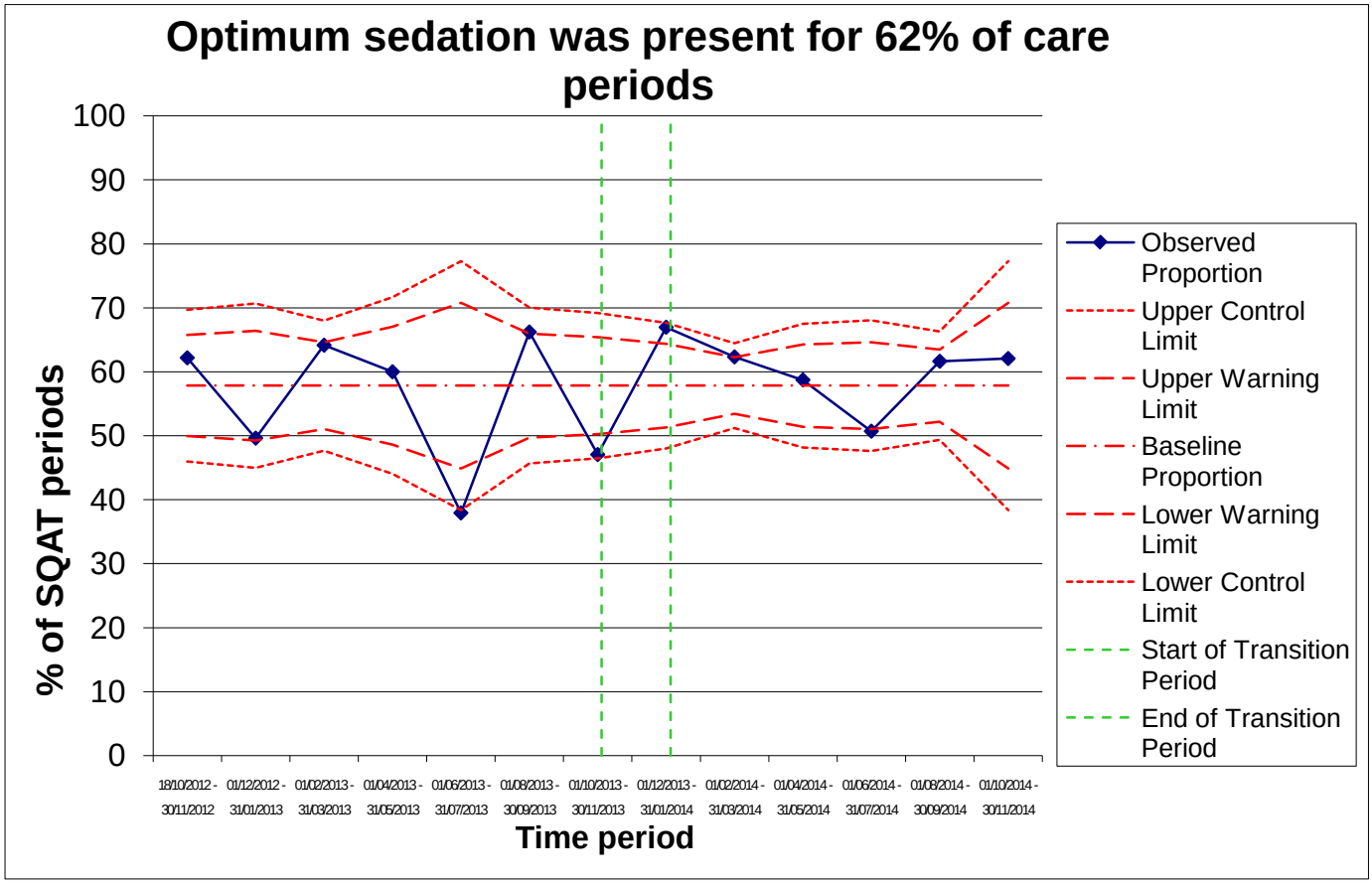
Poor ventilator synchronisation is a common cause of agitation. To learn more access the DESIST LearnPro education package module 6 (*managing agitation*).

"Proportion of periods with optimum sedation"

How was this chart made?

The data recorded by nurses on the SQAT form at the end of each shift was used to generate a measure of overall optimum sedation.

Optimum sedation is defined as a care period (12 hour nursing shift) for which there was no excessive sedation or agitation or poorly relaxed patient or poor ventilator synchronisation. These patients should be awake or rousable, non-agitated, and comfortable on the ventilator, unless there is a clinical reason for keeping them deeply sedated.



What does this chart mean?

The **proportion** is the average rate of this quality measure that occurred in the the ICU during the intervention period October to November 2014 in the DESIST study. **This means that for 62% of care periods in the ICU optimum sedation was present, using the DESIST definition.**

The **observed proportion** is the rate of optimum sedation over 2 months of observations in the the ICU. If the proportion moves closer to the **upper warning or control limit**, the occurrence of optimum sedation is increasing. If it crosses the **upper control limit** this represents a significant increase in optimum sedation in your ICU. If the proportion moves closer to the **lower warning or control limit**, the occurrence of optimum

sedation is decreasing. If it crosses the **lower control limit** this represents a significant decrease in optimum sedation in your ICU.

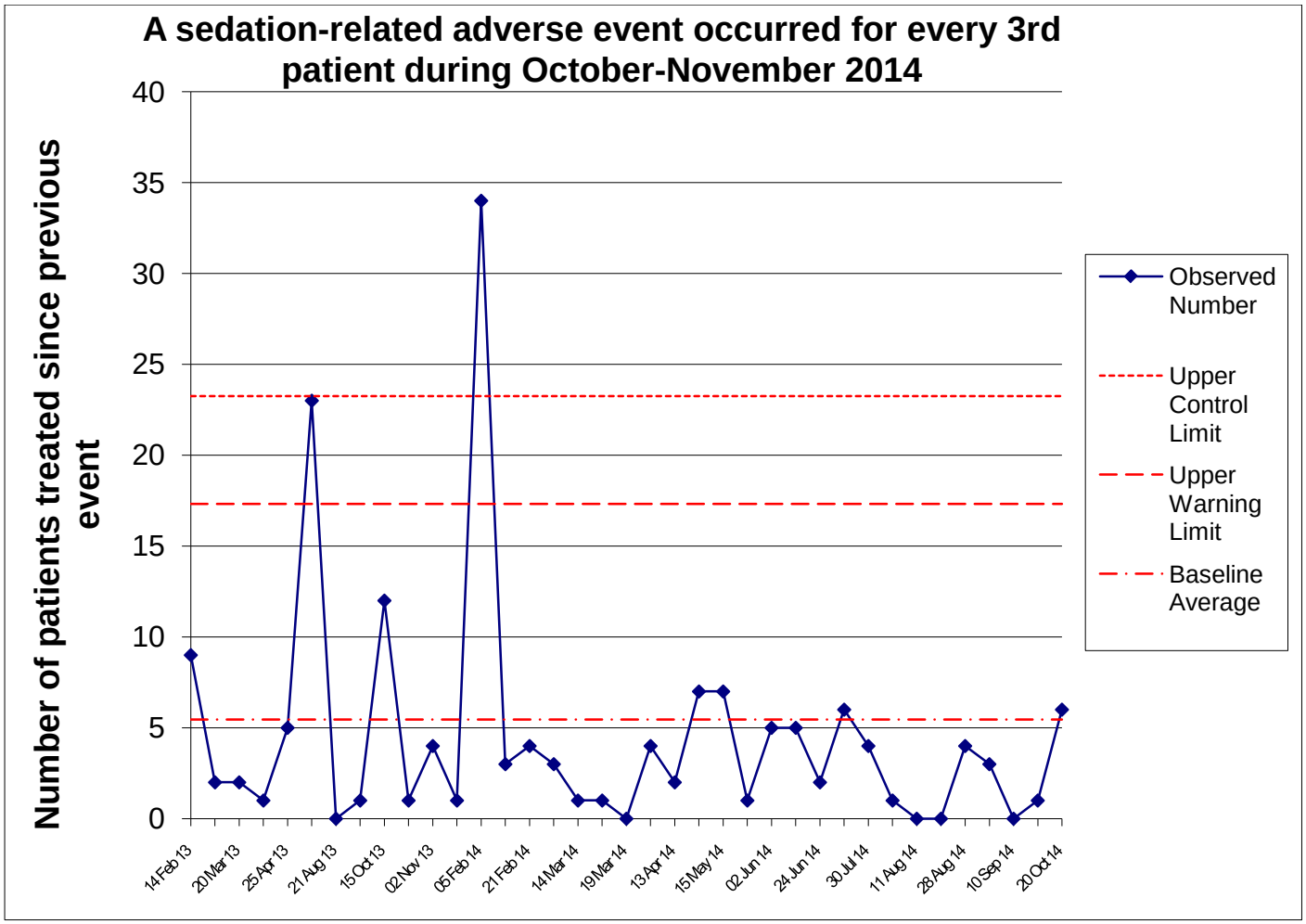
This chart suggests there has been INCREASE in optimum sedation during the period October to November 2014. This is largely due to DECREASE in agitation rate.

To learn more about the importance of optimum sedation access the DESIST LearnPro education package module 1 (*Why is it important to get sedation right*?).

"Number of patients treated without a sedation-related adverse event"

How was this chart made?

In the DESIST study data concerning sedation-related adverse events are collected and recorded on a daily basis. For all sequential patients admitted to your ICU and enrolled in the DESIST study these daily data have been used to create this chart. If an adverse event was recorded during an admission this patient was counted as a patient with a "sedation-related adverse event". We have counted all the sequential patients enrolled in the DESIST study in your ICU between each patient in whom a sedation-related adverse event was recorded. The number of patients is recorded on the Y-axis, and the actual dates on which patients admitted experienced an adverse event on the X-axis.



What does this chart mean?

If the rate of sedation-related adverse events is decreasing, there should be more "higher spikes" in the chart, because this means more patients were treated without an adverse event occurring.

The **average** is the average rate of this quality measure that occurred in the the ICU during the intervention period October to November 2014 in the DESIST study. On average, a **sedation-related adverse event occurred for every 3rd patient during that period.**

If the data points move closer to the **upper control or warning limit**, the rate of sedation-related adverse events is *decreasing*. If it crosses the **upper control limit** this represents a significant decrease compared to the baseline data, which probably means the rate of sedation-related adverse events has significantly decreased in your ICU.

Sedation-related adverse events

The number of several pre-defined sedation-related adverse events was recorded on a daily basis for patients participating in the DESIST study. An awareness of the events occurring in your ICU may allow you to plan changes and interventions to reduce adverse event rates. For example, you may review these in real time at local quality improvement or "M&M meetings" to explore why they are occurring. For the period October to November 2014, there were 4 sedation-related adverse events in the ICU.

Total adverse events occurring during last two months period (October-November 2014)

Type of Sedation-Related Adverse Events	**Number**
Unplanned NG removal	2
Unplanned line removal (central)	1
Unplanned extubation	1
Total	**4**